15



## THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

- 1. A method of reducing or overcoming acquired or inherent cellular resistance to cytotoxic or antineoplastic agents, comprising the step of co-administering systemically to a patient in need thereof an effective amount of said agent together with hyaluronan, wherein said agent is more cytotoxically or anti-neoplastically effective than compared to the same amount of agent alone.
- A method according to claim 1, wherein the agent is selected from the group consisting of methotrexate, paclitaxel (taxol), 5-fluorouracil and cyclophosphamide or combinations thereof.
  - 3. A method according to claim 2, wherein said agent is combined with hyaluronan such that the agent is entrained and/or bound by said hyaluronan.
- 20 4. A method according to claim 3, wherein said combined agent and hyaluronan is capable of binding to receptors on the resistant cell.
- 5. A method according to claim 3, wherein said
  combined agent and hyaluronan is capable of entering a
  resistant cell via bulk endocytosis, wherein said agent is
  delivered into the cell, thereby allowing it to become
  therapeutically active.
- 30 6. A method according to claim 1, wherein the acquired or inherent cellular resistance is associated with a drug-resistant disease.
- 7. A method according to claim 6, wherein the drug35 resistant disease is a drug-resistant cancer.
  - 8. A method for the reduction of gastrointestinal





toxicity of a drug, comprising the step of co-administering systemically to a patient in need thereof an effective amount of said agent together with hyaluronan, wherein said agent has reduced gastrointestinal toxicity when compared to the same amount of the agent alone.

9. A pharmaceutical composition for reducing or overcoming acquired or inherent cellular resistance to cytotoxic or anti-neoplastic agents comprising:

hyaluronan, having a molecular weight greater than 700,000 Daltons, and

a cytotoxic or anti-neoplastic agent, wherein said composition is administered systemically to a patient in need thereof and is more cytotoxically or anti-neoplastically effective than compared to said agent alone, with the proviso that when the agent is paclitaxel the molecular weight of hyaluronan is greater than 750,000 Daltons.

20

15

10